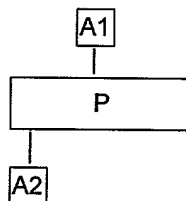


5. (Amended) A method according to claim 1, in which the cycle is a bicycle.
6. (Amended) A method according to claim 1, in which the cycle comprises more than two rings.
7. (Amended) A method according to claim 1, in which the compound is of General Formula II, and the linker L is attached to a backbone nitrogen or to an atom in the side chain of the monomer.
8. (Amended) A method according to claim 1, which is carried out in solution, comprising the steps of:
- a) Preparing a linear peptide of General Formula III



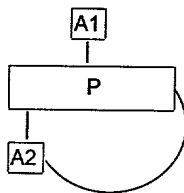
General Formula III

where P is a linear peptide of 1 to 15 monomers;

A1 is one or more N-substituents, either reversible or non-reversible, on the peptide backbone, or is a chemical moiety that forces a *cis* conformation of the backbone, and

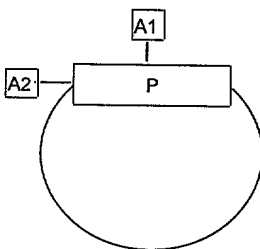
A2 is a covalently-bonded group of atoms comprising a reactive functionality to form an initial large cyclic peptide prior to ring contraction to the desired substituted cyclic peptide;

- b) Activating the C-terminus to form a cyclic peptide of General Formula IV:



General Formula IV

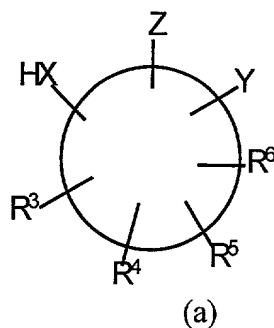
- c) the peptide of General Formula IV to rearrange via a ring contraction reaction (which may occur spontaneously) to form a cyclic peptide of General Formula V; and optionally



General Formula V

- d) Subjecting the cyclic peptide of General Formula V to a deprotection reaction to remove the groups A1 and A2 to yield the desired cyclic peptide of General Formula I.

11. (Amended) A method according to claim 8, in which A1 and/or A2 is left attached to the peptide.
13. (Amended) A method according to claim 8, in which A1 is a reversible N-substituent.
15. (Amended) A method according to claim 8, in which A2 is eliminated by spontaneous ring contraction.
16. (Amended) A method according to claim 8, in which A2 comprises a nucleophile that reacts rapidly with a C-terminus to form an initial large ring, which then contracts either spontaneously, or upon heating or additional chemical treatment.
18. (Amended) A method according to claim 8, in which A2 is an irreversible substituent, is removed after ring contraction, or is eliminated spontaneously upon ring contraction.
19. (Amended) A method according to claim 8, in which A2 is a compound of general formula (a):



in which the ring

- (a) optionally comprises one or more heteroatoms selected from the group consisting of nitrogen, oxygen, and sulphur;
- (b) is of 5 to 7 atoms;
- (c) comprises 3 carbon atoms substituted respectively by XH, Z, and Y; and
- (d) is additionally substituted by groups  $R^3$  and  $R^4$  when the compound is a 5-membered ring, or is additionally substituted by groups  $R^3$ ,  $R^4$ , and  $R^5$  when the compound is a 6-membered ring, or is additionally substituted by groups  $R^3$ ,  $R^4$ ,  $R^5$  and  $R^6$  when the compound is a 7-membered ring,

in which

X is oxygen, sulphur,  $\text{CH}_2\text{O}-$ , or  $\text{CH}_2\text{S}-$ ;

Y is an electron-withdrawing group;

Z is any group which allows the formation of a covalent carbon-nitrogen bond; and

$R^3$ ,  $R^4$  and  $R^5$  are each independently hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, arylalkyl, substituted arylalkyl, heteroaryl, substituted heteroaryl, alkoxy, aryloxy, XH or Y, or a covalent linkage to a solid support, and

in which R<sup>3</sup> and R<sup>4</sup> or R<sup>4</sup> and R<sup>5</sup> can optionally together with the ring form a 5-, 6-, or 7-membered ring.

21. (Amended) A method according to claim 20, in which the linker L is attached to a backbone nitrogen or an atom in the side chain of the monomer.

22. (Amended) A method according to claim 20, in which the cycle is a monocycle.

23. (Amended) A method according to claim 20, in which the cycle is a bicycle.

24. (Amended) A method according to claim 20, in which the cycle comprises more than two rings.

25. (Amended) A method according to claim 20, in which side chain deprotection of the peptide, removal of A1 and cleavage from the solid support are performed separately.

26. (Amended) A method according to claim 20, in which side chain deprotection of the peptide, removal of A1 and cleavage from the resin are performed concurrently.

30. (Amended) A method according to claim 28, in which side chain deprotection of the peptide, removal of A1 and cleavage from the resin are performed separately.

31. (Amended) A method according to claim 28, in which side chain deprotection of the peptide, removal of A1 and cleavage from the solid support are performed concurrently.

36. (Amended) A method according to claim 1, in which one or more of the monomers carries a side chain protecting group.

Please add new claims 37-43, as follows:

37. (New) A method according to claim 20, in which one or more of the monomers carries a side chain protecting group.

38. (New) A method according to claim 27, in which one or more of the monomers carries a side chain protecting group.

39. (New) A method according to claim 32, in which one or more of the monomers carries a side chain protecting group.

40. (New) A method according to claim 33, in which one or more of the monomers carries a side chain protecting group.

41. (New) cyclo [Tyr-Arg-D-Phe Gly].

42. (New) cyclo [Tyr-Arg-Phe-Gly].

43. (New) A composition comprising a cyclo [Tyr-Arg-D-Phe Gly] and/or cyclo [Tyr-Arg-Phe-Gly], together with a pharmaceutically acceptable carrier.

## REMARKS

### **I. Nationalization**

This application represents the U.S. national stage of International Patent Application PCT/AU99/00813, filed September 24, 1999, which claims priority to Australian Patent Application PP 6164, filed September 25, 1998.

As the text of the International Application was transmitted by the International Bureau, an additional copy is not required to satisfy 35 U.S.C. § 371(c)(2). Nonetheless, for the Examiner's convenience, a copy of international application PCT/AU99/00813 is enclosed in the form of the published PCT Application WO 00/18790.

No amendments were made to the application during PCT examination. The claims included with the published PCT Application (all novel and inventive) therefore form the basis for the present claim amendments, of a procedural nature, for entry into the U.S. national stage.

Should formal amendments to the specification be necessary to conform to U.S. practice, Applicants seek to introduce such amendments into the present specification by, *e.g.*, deleting the PCT cover page, providing the Abstract as a separate page, and deleting the PCT header. The amended abstract included herewith complies with the new rules, as it is 200 words.

Priority is also properly claimed by an amendment at page 1.

### **II. National Stage Claims**

After according a U.S. filing date, and **before** calculating the filing fee, entry of the foregoing claim amendments and additional claims is respectfully requested.